

# The Distribution of Vitamin A in Cells of Normal and Pathologic Human Livers

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IT HAS been well demonstrated that the liver is the principal storehouse for vitamin A in man. The content of vitamin A in normal human liver has been shown to vary widely between different subjects. Ellison and Moore<sup>1</sup> have reported normal values to range between 75 to 590, with an average of 220 International Units (IU) per gram. Ralli and co-workers<sup>2</sup> found a mean normal value of 766, with a standard deviation of 625 IU. The cause of this variation is perhaps largely due to differences in the amount of vitamin A ingested. In the normal newborn infant Lewis *et al.*<sup>3</sup> have submitted analyses averaging about 115 IU per gram. The level of vitamin A in these infants is perhaps largely affected by the maternal intake of the vitamin.

Ralli and associates have made an extensive study of the vitamin A content of various pathologic livers and reported a significant decline in the *liver* vitamin A content in many diseases. It is common knowledge also that the vitamin A level of the *blood* is decreased in various diseased conditions.<sup>4</sup> However, the relationship between the amount of vitamin A in the liver and the corresponding blood level has not been clearly defined.<sup>5</sup>

Because we know so little about the factors concerned with the mobilization and metabolism of vitamin A by the liver, it was believed worthwhile to investigate its distribution in the hepatic cells of man in the normal and diseased state.

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## MATERIAL AND METHODS

In the present study the livers of 11 subjects were fractionated and analyzed. The material was obtained at autopsy.\* Seven of the subjects were adults and four were infants. Seven of the liver specimens exhibited no pathologic changes. The total vitamin A and the separation of the alcohol and ester fractions were determined according to the methods of Hjarde<sup>6</sup> and Eden,<sup>7</sup> respectively.

In general, the fractionation procedure was to separate the liver cells into three fractions and to determine the vitamin A content of these fractions as well as that of the whole cell.

The livers were homogenized in 0.25 M sucrose; and cytoplasmic fractions were made by differential centrifugation according to the method of Schneider,<sup>8</sup> as modified in this laboratory.<sup>9</sup> Three fractions were prepared and designated as nuclei, mitochondria, and fraction X. (Fraction X consisted of the remaining cytoplasm after nuclei and mitochondria were removed.†)

Samples of the liver were obtained in all instances within approximately 24 hours and stored at  $-20^{\circ}$  C. The tissues were analyzed within 48 hours after storage.

## RESULTS

The vitamin A content in normal and pathologic liver specimens are presented in Table I.

\* The samples of liver were secured through Drs. M. L. Hobbs, W. A. Ehrigott, and D. Z. Morgan of the Department of Pathology, West Virginia University, School of Medicine.

† Ganguly<sup>10</sup> recently has questioned our method of cell fractionation on the grounds that the nuclear and mitochondrial fractions were contaminated with fraction X during decantation. We followed his suggestion, removing the supernatant fraction with a syringe and needle, but found no significant change in our results.

Although there is considerable variation between the vitamin A content of normal livers and diseased livers, it may be noted that as a group the diseased livers contained less vitamin A than normal livers. A similar finding may be seen for normal and abnormal infant

agreement with those published elsewhere. These data also confirm previous observations that diseases of the liver result in a lowered concentration of vitamin A in this organ. Disease of liver cells, however, does not appear to alter the fractional intracellular distribution of

TABLE I  
The Vitamin A Content in Normal and Pathologic Liver

Subject number	Cause of death	Age	Sex	Vitamin A*/g liver	Per cent vitamin A ester	Per cent vitamin A alcohol
Normal Livers						
1	Myocardial infarction	31	Male	395	90	10
2	Myocardial infarction	41	Male	93	91	9
3	Pulmonary thrombosis	65	Female	135	94	6
4	Arteriosclerotic heart disease	58	Male	352	94	6
5	Anesthetic death	3	Female	172	92	8
Average				229	92	8
Normal Infant Livers						
6	Hyaline membrane	Infant <sup>1</sup>	Female	62	95	5
7	Hyaline membrane	Infant <sup>2</sup>	Female	32	95	5
Livers with Lesions						
8	Arteriosclerotic <sup>3</sup> heart disease	66	Male	43	97	3
9	Carcinoma of pancreas <sup>4</sup>	70	Male	109	97	3
10	Cerebral hemorrhage <sup>5</sup>	27	Male	13	98	2
Average				55	97	3
Infant Liver with Lesions						
11	Stillborn <sup>6</sup>	Infant	Female	28	97	3

\* Three-tenths microgram vitamin A equal to 1.0 International Unit.

<sup>1, 2</sup> Full term—4 days postpartum.

<sup>3, 4, 5</sup> Liver lesions—fatty changes.

<sup>4</sup> Liver lesions—Metastatic infiltration.

livers. The per cent distribution of the ester and alcohol forms showed the alcohol form to be higher in normal than in pathologic livers.

The distribution of vitamin A in normal and pathologic hepatic cells is summarized in Table II. As may be seen, the greatest concentration of vitamin A is in fraction X. Nuclei and mitochondria are next in order of decreasing concentration. There was no significant difference found in the intracellular distribution of vitamin A in normal and pathologic livers. Likewise, there was no difference between infant and adult livers.

#### COMMENT

The level of vitamin A found in our study of normal livers from adults and infants is in

this vitamin. It seems that as the liver loses vitamin A it is not preferentially lost from any one fraction. In this small series the age of the subject had no significant effect upon the intracellular distribution of this compound. This study would suggest that no one cellular fraction is concerned primarily with either the mobilization or storage of vitamin A in man.

#### SUMMARY

Cells in pathologic livers contain uniformly less vitamin A than those in normal livers. The alcohol form of vitamin A is more concentrated in normal than in diseased hepatic cells. The distribution of vitamin A between the various liver cell fractions does not seem to be affected by either age or disease.

TABLE II

The Distribution of Vitamin A in Normal and Pathologic Liver Cells

Per cent vitamin A found in cell fractions <sup>1</sup>				
Subject Number	Fraction X	Nuclei	Mitochondria	Per cent <sup>2</sup> recovery
Normal Livers				
1	62	30	8	93
2	68	29	3	97
3	56	40	4	99
4	50	44	6	97
5	44	53	3	100
Average	56	39	5	97
Normal Infant Livers				
6	58	39	5	101
7	44	50	6	100
Livers with Lesions				
8	55	43	2	95
9	52	45	4	92
10	79	14	7	107
Average	62	34	4	98
Infant Liver with Lesions				
11	31	28	8	90

<sup>1</sup> The per cent distribution is equal to the amount in fraction, divided by the amount in (nuclei + mitochondria + fraction X).

<sup>2</sup> Per cent recovery = sum of nuclei, mitochondria and fraction X, divided by the equivalent amount of total liver.

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